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09/846,058	04/30/2001	Jay K.. Bass	10004190-1	4485

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EXAMINER
EPPERSON, JON D

ART UNIT	PAPER NUMBER
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/846,058	BASS ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,29,31,35 and 37-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28, 29, 31, 35 and 37-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. The Response filed September 26, 2006 is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

Status of the Claims

3. Claims 28, 29, 31, 35 and 37-45 were pending. Applicants amended claim 28 and 45. No claims were amended or canceled. Therefore, claims 28, 29, 31, 35 and 37-45 are currently pending and examined on the merits.

General Comments

4. The following comments are noted:

Applicants state, "there appears to be no reason why these rejections [i.e., the rejections under 35 U.S.C. 112, first paragraph (and also the second paragraph rejection)] could not have been made in the first Office Action over three years ago, or one of the five intervening Office Actions" (e.g., see 9/26/06 Response, page 6, last two paragraphs). In addition Applicants note that "piecemeal" prosecution should be avoided when possible because it "decrease examination efficiency and increase the Applicants' prosecution costs" citing MPEP § 707.07(g) in support of this position (e.g., see 9/26/06 Response, page 7, paragraphs 1 and 2).

While the Examiner agrees that "piecemeal" prosecution should be avoided when possible, the failure to previously cite Smith, B. G., Donald, I. W., Lauf et al., etc. in a 112, first paragraph rejection as set forth below was unintentional. The issue was reconsidered when the examiner was discussing potential amendments to place the case in condition for allowance (e.g., see 7/18/06 Interview Summary). The Examiner regrets any additional expense and, to that end, has tried to make the process fair to Applicants by making the previous action non-final in accordance with MPEP § 706.07.

Withdrawn Objections/Rejections

5. The rejection to claims 28 and 45 under 35 U.S.C. § 112, second paragraph is hereby withdrawn in view of Applicants' amendments thereto. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claim Rejections - 35 USC § 112, first paragraph

6. Claims 28, 29, 31, 35 and 37-45 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a written description rejection.

Applicant's claims are directed to a broad genus of methods for fabricating arrays with different chemical moieties. All the methods employ the use of a substrate. However, the specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form said substrate. Thus, the claims encompass the use of virtually an infinite number of substrates whether they can be transformed into a substrate that contains a higher height uniformity in one direction or not (e.g., see claim 28; see also specification, page 21, line 20, "The substrates may be fabricated from any of a variety of materials"). In addition, the methods encompass substrates that do not possess a first direction that has higher height uniformity than a second direction as required by independent claims 28, 37, 38 and 45. For example, the claims encompass the use of substrates with "random" topology (e.g., see Smith, B. G. "Geometrical Shadowing of a Random Rough Surface" IEEE Transactions on Antennas and Propagation 1967, 5, 668-671; see also Bromberg, L. "Properties of Aqueous Solutions and Gels of Poly(ethylene oxide)-b-poly(propylene oxide)-b-poly(ethylene oxide)-g-poly(acrylic acid)" *J. Phys. Chem. B* **1998**, *102*, 10736-10744 wherein pluronic gels are formed by random hydrophobic interactions) that would not be amendable to current process because the comparison would not produce a definitive result (i.e., a direction with higher height uniformity). In addition, Applicants' claims encompass substrates that likewise cannot possess a first direction that has higher height uniformity than a second direction planar to said substrate. For example, the claims encompass "spherical" substrates (e.g., see also specification, page 9, lines 29 and 30, "Similarly, substrate 10 may be of any shape"; see also specification, page 21,

paragraph 1) that possess tangential planar surfaces that would not foster a comparison of height uniformity because there is only one point at which a plane touches a sphere (i.e., the tangential plane). Furthermore, Applicants' claims encompass many substrates that cannot be "drawn" into shapes that possesses height uniformity because these materials are either too brittle or would react with other materials at the melting temperature required for fabrication (e.g., see Donald, I. W. "Production, properties and applications of microwire and related products" *J. Mater. Sci.* **1987**, *22*, 2661-2679, see especially, page 2665, section 2.1.2.3). Finally, no structural limitations are placed on the "chemical moieties" that are used to form the array either. Thus, virtually an infinite number of chemical moieties are also being claimed wherein no structural features and/or common structural characteristics are set forth (e.g., see Lauf et al., page 1, paragraph 4, "The preparation of new materials with novel and useful chemical and/or physical properties is at best unpredictable considering current levels of understanding. Consequently, the discovery of new materials depends largely on the ability to synthesize and analyze new compounds. Given approximately 100 elements in the periodic table, which can be used to make compositions consisting of three, four, five, six or more elements, the universe of possible new compounds remains largely unexplored.").

In contrast, Applicant's specification sets forth only one working example of a substrate with higher height uniformity in one direction than in another (e.g., see specification, page 3, paragraph 2; see also figures 6 and 7 wherein a planar glass substrate that was drawn in the molten state through a thin slot is set forth). Although the Applicants mention several other species that might be possible (e.g., see specification,

page 21, paragraph 2 wherein both flexible and non-flexible materials are set forth including nylon, nitrocellulose, polypropylene, etc.), there is no evidence that any of these substrates were ever made and/or tested. Furthermore, there is no evidence presented that would suggest that any or all of the materials would likewise be amendable to a rolling process (like the one set forth for the drawn glass) that would impart a higher height uniformity. In addition, Applicants do not set forth any working examples of a chemical moiety. Although the specification sets forth several potential species (e.g., biopolymers such as carbohydrates, see specification, page 6, last paragraph) and cite several references such as Ser. No. 09/302898 for "Polynucleotide Array Fabrication", there is no evidence that any of these chemical moieties were ever used in accordance with the claimed method. Thus, Applicants have not even set forth a single working example of the claimed method when the chemical entities are taken into account (i.e., no quid pro quo here).

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the claimed invention (e.g., see *In re Edwards*, 568 F.2d 1349, 1351-52, 196 USPQ 465, 467 (CCPA 1978); see also see also *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111 (CAFC 1991)). The "written description" requirement may be satisfied by using "such descriptive means as words, structures, figures, diagrams formulas, etc., that fully set forth the claimed invention" (e.g., see *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966). In the present case, Applicants have not set forth even a single working example of the present invention. In addition, when there is *substantial variation within*

the genus, one must describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05). Here, the variation within the genus would be enormous because the nature of the claimed methods would depend on the nature of the substrates employed, which are virtually limitless. Furthermore, the vast numbers of substrates do not share any common attributes that would allow a person of skill in the art to extrapolate Applicants' limited species to he vast number of currently claimed substrates. Thus, the general knowledge and level of skill in the art do not supplement the omitted description because no known structure/function relationship and/or chemical properties exists that could otherwise be used to show possession of the enormous genus. In addition, there is no known generally accepted method for producing this wide array of substrates. Thus, the claims fail to satisfy the constitutional requisite of promoting the progress of science and the useful arts since this seeks to monopolize all possible ways to achieve a given result (e.g., all substrates), far beyond those means actually discovered or contemplated by the inventor (e.g., molten glass drawn into a flat rectangular shape), so that others would have no incentive thereafter to explore a field already fully dominated. *O'Reilly v. Morse*, 15 How. 62, *In re Fuetterer*, 50 CCPA 1453, 1963 C.D. 620, 795 O.G. 783, 319 F.2d 259, 138 USPQ 217; *Siegel v. Watson*, 105 U.S. Appl. D.C. 344, 1959 C.D. 107, 742 O.G 863, 267 F.2d 621, 121 USPQ 119.

Response

7. Applicant's arguments directed to the above written description rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed

persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, " the Examiner is apparently applying an improper standard for written description. The claims contain an operability element by virtue of reciting *a method of fabricating an array of multiple features of different chemical moieties on a substrate surface*. Therefore, inoperative embodiments that cannot be used to practice this method are not included within the scope of the claim. Union Carbide Chemicals & Plastics Tech. Cbrp v. Shell Oil Co., 308 F .3d 1 167 (CAFC 2002). Inoperative embodiments not included in the claims need not be described, as the Examiner appears to be requiring" (e.g., see 9/26/06 Response, paragraph bridging pages 8 and 9).

[1] The Examiner respectfully disagrees. Applicants statement "a method of fabricating an array of multiple feature of different chemical moieties on a substrate surface" does not constitute an "operability element" because it does not insure that such an array will contain multiple features "more closely aligned" with a first direction than a second direction. For example, the claim doesn't read "*A method of fabricating an array of multiple features of different chemical moieties on a surface of a substrate wherein said multiple features are more closely aligned in a first direction having higher substrate height uniformity than a second.*" Thus, inoperative embodiments that place different chemical moieties at "random" positions on the surface of the substrate are not excluded by this phrase.

[2] Applicants argue, "the Court has held that it is not a function of the claims to specifically exclude possible inoperative embodiments" and cite Atlas Powder Co. in support of this position. (e.g., see 9/26/06 Response, page 9, paragraphs 1 and 2).

[2] The Examiner agrees that inoperative embodiments may be included in accordance with Atlas Powder Co. However, [I]f the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid." Atlas Powder Co. v. E.I. DuPont de Nemours & Co., 750 F.2d 1569, 1576-77, 224 USPQ 409, 414 (Fed. Cir. 1984). Here, the number of non-operative embodiments is enormous. For example, Applicants are claiming virtually every known substrate including "rigid" materials (e.g., see specification, page 21, lines 20-30, "The substrates may be fabricated from any of a variety of materials ... including "rigid" substrates"). However, this broad definition includes substrates that cannot be "drawn" into shapes that possesses higher height uniformity (e.g., see figures 5, 6, and 8) because these materials are either too brittle or would react with other materials at the melting temperature required for fabrication (e.g., see Donald, I. W. "Production, properties and applications of microwire and related products" J. Mater. Sci. 1987, 22, 2661-2679, see especially, page 2665, section 2.1.2.3). This evidence has not been contested by Applicants. In addition, the claims encompass substrates "any shape" (e.g., see specification, page 21, paragraph 1), which would encompass, for example, "spherical" shapes. It would be impossible to "identify a first direction having higher substrate height uniformity than a second direction, wherein said first and second directions are

planar" (e.g., see claim 28) because a plane only touches a sphere at a single point (i.e., a tangential plane). Therefore, not "all shapes" are adequately described. Again, Applicants did not contest this point. In addition, and perhaps most importantly, Applicants' claims do NOT require a "drawing" step that might impart higher height uniformity to the substrate (e.g., see claim 28, see also 9/26/06 Response, page 10, paragraph 1, "The claims are not drawn to making a substrate [i.e., drawing method]; they imply that the substrate already has been made") (emphasis added). Thus, most substrates used "as is" would exhibit a "random" topology as evidence by Smith, B. G. (see above) and could not be used. That is, a comparison of a first and second direction would not produce a definitive result because a direction with higher height uniformity does not exist. This point also has not been contested. "[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art." See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)). That is clearly not the case for the reasons set forth above.

[3] Applicants argue, "the written description requirement and enablement requirements 'usually rise and fall together. That is, a recitation of how to make and use the invention across the full breadth of the claim is ordinarily sufficient to demonstrate that the inventor possesses the full scope of the invention, and vice versa.' … Therefore, if a claim is enabled, it is described" citing Lizardtech, Inc. v. Earth Resource Mapping among others in support of this position (e.g., see 9/26/06 Response, page 9, paragraph 3).

[3] "Although the two concepts are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures the that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30,2001) citing University of California v. Eli Lilly & Co. Therefore, the do not necessarily "rise and fall together" as purported. In any event, Applicants' claims are not enabled (see below), which renders this argument moot.

[4] Applicants argue, "The facts of Applicants' Invention and the elements of Applicants' claims themselves provide sufficient guidance to exclude many inoperative embodiments. Those substrates that cannot possess the directional and 'height uniformity elements … are not included within those claims." (e.g., see 9/26/06 Response, page 9, last paragraph).

[4] The Examiner respectfully disagrees. Nothing in the claims or specification provides support for this position. To the contrary, Applicants expressly set forth "broad" definitions for what constitutes a substrate (e.g., "wide variety" of materials of "any shape"). The claims (and other portions of the specification) have not contradicted this express language and Applicants' lack of cited passages in support of this argument reflects this.

[5] Applicants argue, "Applicants have disclosed a list of suitable substrate materials" (e.g., see 9/26/06 Response, page 10, paragraph 1).

[5] The list is merely "exemplary" and does not exclude any of the inoperative embodiments set forth above.

[6] Applicants argue, "The claims are not drawn to making a substrate; they imply that the substrate already has been made." (e.g., see 9/26/06 Response, page 10, paragraph 1).

[6] This is one of the main reasons that the Examiner has concluded that Applicants' are not in possession of the claimed invention (see section [2] above, part where emphasis was added).

[7] Applicants argue, "Materials that cannot form substrates or those that cannot be used to make substrates with the directional and height uniformity elements of Applicants' claims are known to a person skilled in the materials art. In addition, such materials are excluded from the claims because the claims require that such a substrate exist." (e.g., see 9/26/06 Response, page 10, paragraph 1).

[7] The Examiner respectfully disagrees. See sections [4] and [5] above.

[8] Applicants argue, "One would infer from the operability element of the claims (a method of fabricating an array of multiple features of different chemical moieties on a substrate surface) that the chemicals actually form features. One skilled in the array art would know not to deposit chemicals that cannot be useful with array technology or those that cannot form features. Chemicals without these criteria are excluded from the claims as inoperative." (e.g., see 9/26/06 Response, page 10, paragraph 2).

[8] As in section [4] above, all evidence is to the contrary. Applicants only imply that the multiple features must be of a "chemical" nature (e.g., see claim 28, "A method of fabricating an array of multiple features of different chemical moieties), which would include virtually an infinite number of materials. According to Lauf, most of the materials remain "largely unexplored" (e.g., see Lauf et al., page 1, paragraph 4, "The preparation of new materials with novel and useful chemical and/or physical properties is at best unpredictable considering current levels of understanding. Consequently, the discovery of new materials depends largely on the ability to synthesize and analyze new compounds. Given approximately 100 elements in the periodic table, which can be used to make compositions consisting of three, four, five, six or more elements, the universe of possible new compounds remains largely unexplored."). Again, the Lauf et al. reference has not been contested by Applicants.

[9] Applicants argue, "Two recent court decisions make it clear that a determination of what is needed to describe generic claims depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter … there is no analysis on this record applying the Capon factors, the rejection is improper" (e.g., see 9/26/06 Response, page 10, paragraph 3).

[9] A specification complies with the 35 U.S.C. § 112, first paragraph, written description requirement if it conveys with reasonable clarity to those skilled in the art

that, as of the filing date sought, the inventor was in possession of the invention. See Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-4, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991); In re Kaslow, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983); In re Edwards, 568 F.2d 1349, 1351-2, 196 USPQ 465, 467 (CCPA 1978); In re Wertheim, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). "[T]he PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims." Wertheim, 541 F.2d at 263, 191 USPQ at 97. Here, the Examiner has set forth many reasons, based on a factual inquiry, why a person of skill in the art would not recognize in the disclosure a description of the invention defined by the claims. For example, the Examiner noted that the vast majority of substrates would have a "random" topology that would not be amendable to the presently claimed method (see above arguments and cited references). Likewise, "brittle" substrates or "spherical" materials will not work. Therefore, the Examiner's burden has been met.

Accordingly, the written description rejection cited above is hereby maintained.

8. Claims 28, 29, 31, 35 and 37-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for forming an array of oligonucleotides on a rectangular substrate of drawn glass, does not reasonably provide enablement for methods that will lead to the production of "any" chemical moiety on "any" substrate surface. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". Some of these factors may include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: Applicant's claims are directed to a broad genus of methods for fabricating arrays with different chemical moieties. All the methods employ the use of a substrate. However, the specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form said substrate. Thus, the claims encompass the use of virtually an infinite number of substrates (e.g., see claim 28; see also specification, page 21, line 20, "The substrates may be fabricated from any of a variety of materials"). In addition, the methods encompass substrates that do not possess a first direction that has higher height uniformity than a second direction as required by independent claims 28, 37, 38 and 45. For example, the claims encompass the use of substrates with "random" topology (e.g., see Smith, B. G. "Geometrical Shadowing of a Random Rough Surface" IEEE Transactions on Antennas and Propagation 1967, 5, 668-

671; see also Bromberg, L. "Properties of Aqueous Solutions and Gels of Poly(ethylene oxide)-b-poly(propylene oxide)-b-poly(ethylene oxide)-g-poly(acrylic acid)" *J. Phys. Chem. B* **1998**, *102*, 10736-10744 wherein pluronic gels are formed by random hydrophobic interactions) that would not be amendable to current process because the comparison would not produce a definitive result (i.e., a direction with higher height uniformity). In addition, Applicants' claims encompass substrates that likewise cannot possess a first direction that has higher height uniformity than a second direction planar to said substrate. For example, the claims encompass spherical substrates (e.g., see also specification, page 9, lines 29 and 30, "Similarly, substrate 10 may be of any shape"; see also specification, page 21, paragraph 1) that possess tangential planar surfaces that would not foster a comparison of height uniformity because any comparison of said directions would only provide information with regard to the same point on the substrate (i.e., the point at which the plane touches the sphere). Furthermore, Applicants' claims encompass many substrates that cannot be "drawn" into shapes that possesses height uniformity because these materials are either too brittle or would react with other materials at the melting temperature required for fabrication (e.g., see Donald, I. W. "Production, properties and applications of microwire and related products" *J. Mater. Sci.* **1987**, *22*, 2661-2679). Finally, no structural limitations are placed on the "chemical moieties" that are used to form the array either. Thus, virtually an infinite number of chemical moieties are also being claimed wherein no structural features and/or common structural characteristics are set forth. Consequently, the nature of the invention cannot be fully determined because the invention has not been defined with particularity.

(3 and 5) The state of the prior art and the level of predictability in the art: The level of predictability in the art is low or absent. For example, the methods encompass substrates that do not possess a first direction that has higher height uniformity than a second direction as required by independent claims 28, 37, 38 and 45. For example, the claims encompass the use of substrates with "random" topology (e.g., see Smith, B. G. "Geometrical Shadowing of a Random Rough Surface" IEEE Transactions on Antennas and Propagation 1967, 5, 668-671; see also Bromberg, L. "Properties of Aqueous Solutions and Gels of Poly(ethylene oxide)-b-poly(propylene oxide)-b-poly(ethylene oxide)-g-poly(acrylic acid)" *J. Phys. Chem. B* **1998**, *102*, 10736-10744 wherein pluronic gels are formed by random hydrophobic interactions) that would not be amendable to current process because the comparison would not produce a definitive result (i.e., a direction with higher height uniformity) and thus represent "inoperative" embodiments because the claimed comparison will not lead to a definitive result (i.e., one direction will not be better than the other). In addition, substrates that have been "drawn" using a thin slit, for example, which might reasonably be expected to produce a direction with higher height uniformity does not encompass all substrates. For example, Applicants' claims encompass many substrates that cannot be "drawn" into shapes that possesses height uniformity because these materials are either too brittle or would react with other materials at the melting temperature required for fabrication (e.g., see Donald, I. W. "Production, properties and applications of microwire and related products" *J. Mater. Sci.* **1987**, *22*, 2661-2679, see especially, page 2665, section 2.1.2.3).

In addition, many of Applicants' claimed substrate shapes would likewise be

inoperative. For example, claims encompassing spherical substrates (e.g., see also specification, page 9, lines 29 and 30, "Similarly, substrate 10 may be of any shape"; see also specification, page 21, paragraph 1) that possess tangential planar surfaces would not foster a comparison of height uniformity because any comparison of said directions would only provide information with regard to the same point on the substrate (i.e., the point at which the plane touches the sphere). Thus, no comparative result would be produced.

Finally, there are no known methods that enable the synthesis and/or characterization of the currently claimed chemical moieties (e.g., see Lauf et al., U.S. Patent Application No. 2004/0062911 A1; page 1, paragraph 4, "The preparation of new materials with novel and useful chemical and/or physical properties is at best unpredictable considering current levels of understanding. Consequently, the discovery of new materials depends largely on the ability to synthesize and analyze new compounds. Given approximately 100 elements in the periodic table, which can be used to make compositions consisting of three, four, five, six or more elements, the universe of possible new compounds remains largely unexplored."; see also Newsam, J. M.; Schuth, F. "Combinatorial Approaches as a Component of High-throughput Experimentation (HTE) in Catalysis Research" Comb. Chem. Biotechnol. Bioeng. 1999, 611, 203-216, especially page 210, column 2, paragraphs 2-3 "Applications of HTE [High Throughput Experimentation] and combinatorial methods to heterogeneous catalysts are substantially different from those used in homogeneous catalysis ... First, we have little basis yet for formal library design, atomic-level active-site structure usually being, at best, poorly

characterized. Second, detailed catalysts characterization is difficult. The averaged picture provided by X-ray and neutron scattering or EXAFS usually masks the active-site signatures, and local probes are likely to miss these critical, yet dilute fine details. Third, the optimal performance of a catalysts is a balance between reactor configuration, reaction conditions, and the details of the catalyst itself; a change in one of the three elements requires concomitant adjustment in the two others. Fourth, scale-up of catalyst preparation even from the laboratory scale can be difficult. Firth, many catalysts only attain theri desirable properties after time on stream, catalyst formation and deactivation processes being important in determining performance. Finally, the reaction conditions required for practical testing typically entail elevated temperatures and pressures, and various gas or liquid streams that might be flammable or toxic. Unsurprisingly, therefore, the field of accelerated combinatorial heterogeneous catalysis is still at an early stage of development" as another example of a catalyst library that falls within the scope of Applicants' claimed chemical moieties).

(4) The level of one of ordinary skill: The level of skill required would be high, most likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants have not even provided a single working example of the claimed invention. Although Applicants' specification sets forth only one working example of a substrate with higher height uniformity in one direction than in another (e.g., see specification, page 3, paragraph 2; see also figures 6 and 7 wherein a planar glass substrate that was drawn in the molten state through a thin slot is set forth), it fails to use

this substrate in the claimed method for generating an array. That is, Applicants do not even set forth one working example of an array of chemical moieties. Although the specification sets forth several potential species (e.g., biopolymers) and cite several references such as Ser. No. 09/302898 for "Polynucleotide Array Fabrication", there is no evidence that any of these chemical moieties were ever used in accordance with the claimed method.

(8) The quantity of experimentation needed to make or use the invention base on the content of the disclosure: As a result of the broad and unpredictable nature of the invention and the lack of specific guidance from the specification, the Examiner contends that the quantity of experimentation needed to make and or use the invention would be great. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 * n.23 (Fed. Cir. 19991). In this case, Applicants have not provided any working examples that would teach this enormous genus that falls within a highly unpredictable art area. Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Response

9. Applicant's arguments directed to the above Enablement rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "Applicants' reiterate their arguments above with respect to the rationale that should be used with respect to the exclusion of inoperative embodiments … ." (e.g., see 9/26/06 Response, page 11, paragraphs 2-4).

[1] To the extent that Applicants are merely repeating their previous arguments, the Examiner contends that those issues were adequately addressed in those previous sections (which are incorporated in their entireties herein by reference).

[2] Applicants argue, "Furthermore, the Court has held that it is not a function of the claims to specifically exclude possible inoperative embodiments … ." (e.g., see 9/26/06 Response, page 11, last paragraph).

[2] See section [2] of the written description response above (which is incorporated in its entirety herein by reference), which is equally applicable in the Enablement context here as well.

[3] Applicants argue, "Applicants submit (for the reasons presented above in the arguments against the written description rejection) that the specification evinces that the experimentation required for the exclusion of inoperative embodiments and for the

determination of operative embodiments would be routine, and not undue" (e.g., see 9/26/06 Response, page 12, paragraph 1).

[3] See section [1] above.

[4] Applicants argue, "the Examiner has not established that the claims contain such a significant number of inoperative embodiments that the experimentation for the exclusion of these embodiments and the determination of operative embodiments would be undue, the claims are enabled for the full scope thereof." (e.g., see 9/26/06 Response, page 12, paragraph 1).

[4] The Examiner respectfully disagrees. For example, as stated above, most of the currently claimed embodiments would be inoperable because the claimed methods do not require a "drawing" step that might otherwise impart a higher height uniformity to the substrate. This factual finding alone, as evidenced by Smith, B. G for example, would suggest that most substrates would not be amenable to the presently claimed methods. Logic also dictates that most substrate surfaces will possess a "random" topology (less entropy) unless some force is applied (e.g., a drawing step) to impart a height uniformity. Therefore, it is safe to conclude that most of the currently claimed embodiments are inoperative.

In addition, the case does not fall under Atlas Powder Co. as purported but, rather cases like In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993) because it is a "scope" of enablement rejection. That is, the claims encompass embodiments that are

not enabled at all (i.e., no "spherical" shapes are enabled regardless of what the substrate is made of). No "random" topology is enabled without the use of a "drawing" step. Therefore, a few inoperative embodiments are not "evenly sprinkled" into an enabled genus that might otherwise be difficult to remove from the genus. To the contrary, the claims encompass non-enabled subgenera that do not possess any enabled species. Furthermore, these subgeneric embodiments are easy to remove (e.g., the "spherical embodiments" could be removed by recited a substantially planar substrate; the "random" embodiments could be removed by reciting a "drawing method"). This fact alone, distinguishes Atlas Powder Co. Thus, the claims are not "commensurate in scope" with what is enabled. See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) ("[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.").

Finally, the Examiner notes that Applicants' failed to address any of the references set forth in the rejection. Thus, the evidence favors non-enablement.

Accordingly, the Enablement rejection cited above is hereby maintained.

Claims Rejections - 35 U.S.C. 102

10. Claim 45 is rejected under 35 U.S.C. 102(b) as being anticipated by Cremer et al. (Cremer et al. "Creating spatially addressed Arrays of Planar Supported Fluid Phospholipid Membranes" *J. Am. Chem. Soc.* **1999**, *121*, 8130-8131).

For ***claim 45***, Cremer et al. (see entire document) disclose method for

fabricating an array of planar supported fluid phospholipids membranes (e.g., see Cremer et al, page 8130, column 1; see also figures 1 and 2), which anticipates the claimed invention. For example, Cramer et al. disclose **(a)** comparing height uniformity of a first direction and a second direction across a planar surface of a substrate to identify a first direction having higher height uniformity than a second direction, wherein said first and second directions are planar to said substrate (e.g., see figure 4; see also page 8131, column 2; see also figures 1-3). Here, Cremer et al. measure and compare the height of the chemical features along the surface of the planar chip in all directions. For example the height of the square wells that contain lipids is ~ 5 nm higher than the wells that do not contain a lipid bilayer (e.g., see figure 4). In addition, the hydrophobic barriers between each square well was also measured and ranged between 25 μm to 250 μm in thickness (e.g., see figure 1; see also page 8130, column 1, paragraph 2, see also page 8131, column 2, "Up to now we have experimented with square well plates from 25 μm × 25 μm to 250 μm × 250 μm with hydrophobic partitions ranging from 25 μm to 250 μm in thickness"). Thus, all heights in every direction along the planar surface were measured and compared, which would include a first and second direction. In addition, Cremer et al. disclose **(b)** placing the different chemical moieties in a row on said planar surface of the substrate lengthwise along the direction having the higher height uniformity so as to provide a row of different chemical moieties that is more closely aligned with the first direction than the second direction (e.g., see figures 2 and 3; see also page

8131, column 2). For example, three different dyes or dye mixtures were placed in the leftmost column, which is more closely aligned in a vertical direction as opposed to a slight more skewed angle. Furthermore, this "vertical" positioning is more closely aligned with a direction that has higher height uniformity than a second "skewed" direction that does not (e.g., see 12/29/05 Office Action, page 4, figures A and B showing principle behind difference in heights along the surface of a substrate between vertically aligned, figure A, and skewed angles, figure B). In addition, Cremer et al. disclose rows that contain a plurality of spatially addressable features containing said different chemical moieties (e.g., see figures 2 and 3 showing different chemical moieties that are spatially addressable).

Response

11. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "the Examiner's remarks regarding the height of wells containing lipids indicate that height uniformity was measured after deposition of the lipids. However, Applicants' claim recites that height uniformities of the substrate are compared before placement of the chemical moieties upon the substrate."

[1] The Examiner respectfully disagrees. The well "height" was measured before deposition (e.g., see figure 1 showing "height" of microcapillary above the surface to be 5 μm; see also page 8130, column 1, paragraph 2). In addition, Applicants claims do not require the comparison "before" the placement. Altiris Inc. v. Symantec Corp., 318 F.3d 1363, 1371, 65 USPQ2d 1865, 1869-70 (Fed. Cir. 2003) (Although the specification discussed only a single embodiment, the court held that it was improper to read a specific order of steps into method claims where, as a matter of logic or grammar, the language of the method claims did not impose a specific order on the performance of the method steps, and the specification did not directly or implicitly require a particular order). Here, Applicants' use of "comprising" language does not require that step (a) come before step (b) in claim 45. For example, different chemical moieties could "fortuitously" be placed in a row on said planar surface of the substrate lengthwise along the direction having higher height uniformity being measured thereafter to confirm the proper placement.

[2] Applicants argue, "one would reasonably interpret the disclosure of the 25 μm to 250 μm partition thickness range to mean that a plurality of substrates, each containing the same size partitions were intended, and that all worked equally well." (e.g., see 9/26/06 Response, page 13, second to last paragraph).

[2] Even if the Examiner were to concede this point, it would not change the outcome e.g., see 12/29/05 Office Action, page 4, figures A and B showing principle behind difference in heights along the surface of a substrate between vertically aligned, figure A, and skewed angles, figure B).

[3] Applicants argue, "The Examiner's rejection appears to be based on inherency and on an interpretation of Cremer that amounts to a possibility that different sized partitions are present on a single substrate. The Examiner has not supported the rejection by factual and technical grounds establishing that the inherent feature must flow as a necessary conclusion, not simply a possible conclusion, from the teaching of the cited art. As such, there is no anticipation." (e.g., see 9/26/06 Response, page 13, last paragraph).

[3] The rejection is not based on inherency and, as a result, Applicants' arguments are moot. The "factual basis" referred to by the Examiner's is set forth in the cited figures. The different size partitions, for example, can be seen in figures 1-4 and are explicitly set forth in the text at, for example, page 8131, column 2, which was cited in the above rejection).

[4] Applicants argue, "the Examiner appears to be asserting that Cremer chose between depositing three different dyes vertically, rather than at a slightly more skewed angle. However, there is nothing in Cremer that would indicate that anything but vertical deposition was contemplated" (e.g., 9/26/06 Response, page 14, paragraph 1).

[4] No such assertion has been made and, as a result, Applicants' arguments are moot. Claim 45 does not require a "choice" as implied by Applicants. The claim merely requires the "placement" of different chemical moieties in a certain direction whether they were placed intentionally or fortuitously. Therefore, Applicants' arguments are not commensurate in scope with the claims.

Accordingly, the 35 U.S.C. § 102 rejection cited above is hereby maintained.

Claim Rejections - 35 USC § 103

12. Claims 28 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cremer et al. (Cremer et al. "Creating spatially addressed Arrays of Planar Supported Fluid Phospholipid Membranes" *J. Am. Chem. Soc.* **1999**, *121*, 8130-8131) in view of Lemmo et al. (Lemmo et al. Anal. Chem. **1997**, *69*, 543-551) and Baldeschwieler et al. (WO 95/25116) (Date of Patent is **September 21, 1995**) (2/21/02 IDS, entry 1L).

For ***claim 45***, Cremer et al. teach all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates and, as a result, renders obvious claim 45. Connell v. Sears, Roebuck & Co., 722 F.2d 1542, 1548 (Fed. Cir. 1983) ("anticipation is the epitome of obviousness"); see also see In re Skoner, 517 F.2d 947, 950, 186 USPQ 80, 83 (CCPA 1975); In re Pearson, 494 F.2d 1399, 1402, 181 USPQ 641, 644 (CCPA 1974).

The prior art teachings of Cremer et al. differ from the claimed invention as follows:

For ***claim 28***, Cremer et al. are fails to teach the use of a pulse-jet printer to deposit the different chemical moieties.

However, the combined references of Lemmo et al. and Baldeschwieler et al. teach the following limitations that are deficient in Cremer et al.:

For ***claim 28***, the combined references of Lemmo et al. and Baldeschwieler et al. (see entire documents) teach the use of a pulse-jet printer for the synthesis of

combinatorial libraries (e.g., see Lemmo et al., abstract; see also figure 2; see also page 544, column 1, paragraph 2 wherein piezoelectric devices are disclosed; see also Baldeschwieler et al., figure 2; see also page 16, line 25; see also Example 1; see also Applicants' specification, page 13, paragraph 3, which defines pulsejet printers to include piezoelectric devices commonly found in inkjet printers).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a pulse jet printer as taught by the combined references of Lemmo et al. and Baldeschwieler et al. to make the spatially addressable arrays as taught by Cremer et al. because Cremer et al. state that pulsejet printers can be used for this purpose and explicitly cite the Lemmo et al. in support of this position (e.g., see Cremer et al., page 8131,.column 2, "Incorporating new deposition technologies such as the chemical inkjet microdispenser should allow very large membrane libraries to be created on experimentally practical time scales"). Furthermore, a person of ordinary skill in the art would have been motivated to use a pulsejet printer to create large libraries on an "experimentally practical time scale" (e.g., see Cremer et al., page 8131, column 2). In addition, Cremer et al. state, "the microdispenser could [also] serve as a convenient method for depositing premixed concentration arrays of three or four component membranes" (e.g., see Cremer et al., page 8131, column 2). Moreover, the pulse jet printer represents a "non contact" method of deposition that will not harm the substrate or contaminate adjacent wells. Finally, a person of ordinary skill in the art would reasonably have expected to be successful because inkjet printers were routinely used for making material libraries.

Response

13. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "With regard to claim 45, the Examiner's only rationale for obviousness is that because Cremer anticipates the claim, it renders the claim obvious as a result. Applicants presume that the Examiner perceives some difference between Cremer and Applicants' Claim for there to be a basis for rejection under 35 U.S.C.3 103(a). However, the Examiner has not presented a proper analysis of obviousness under the standard enunciated by the Supreme Court in Graham v. John Deere, 383 U.S. 1, 148 USPQ 459 (1966). Such an analysis includes a recitation of the perceived differences between the claim and the cited art. Applicants are at a loss with regard to responding to this rejection unless they know the proper basis for the rejection. Clarification is respectfully requested."

[1] "[A]nticipation is the epitome of obviousness," Connell v. Sears, Roebuck & Co., 722 F.2d 1542, 1548 (Fed. Cir. 1983) and, as a result, no "differences" need be shown for claim 45.

[2] Applicants argue, "The secondary documents were cited only for their disclosure of using pulse-jet printers in the synthesis of combinatorial libraries. Therefore, the secondary documents do not remedy the deficiency of Cremer because, as pointed out in the rejection under 35 U.S.C. § 102(b), they do nothing to provide the elements missing from Cremer vis-a-vis the rejected claims. The disclosure of pulse-jet printers does not and cannot supply the factual and technical grounds necessary to establish inherency.

[2] To the extent that Applicants are arguing that Cremer et al. is somehow deficient as a 35 U.S.C. § 102(b) reference and that the disclosure of Baldeschwieler et al. does not remedy this deficiency, the Examiner contends that Cremer et al. is not deficient (i.e., missing any elements other than the printer as set forth in the rejection) for the reasons set forth above. Thus, Applicants' arguments are moot.

Accordingly, the 35 U.S.C. § 103(a) rejection cited above is hereby maintained.

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The

examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
December 19, 2006

JON EPPERSON
PRIMARY EXAMINER